

AMIGO-1 Trial Meets 18-Month PFS End Point With Frontline Amivantamab Triplet in *EGFR*+ NSCLC

Phase 2 AMIGO-1

Top-Line Finding

66.7%

vs

~50%

18-month PFS

Amivantamab + lazertinib
+ pemetrexed

Historical benchmark

Osimertinib monotherapy

(FLAURA) $P = .0045$

Key Efficacy Data

Finding	Result
Median PFS	80% (CI, 20.2-NE)
Confirmed ORR	85% (4% complete response)
Median DoR	Not reached (95% CI, 23.6-NR)
18-month OS rate	74.3% (80% CI, 65.4%-81.3%)
18-month lung cancer-specific survival	91.1%

Trial Snapshot



Design

Multicenter, single-arm, phase 2
(13 Brazilian sites)



Primary end point:

18-month PFS rate
Secondary: OS, ORR



Population

54 treatment-naïve patients with
recurrent or metastatic *EGFR*-
mutant NSCLC.
Exon 19 deletion 61%, L858R 39%, brain
metastases at baseline 43%



Regimen:

Amivantamab + lazertinib +
pemetrexed 500 mg/m²
capped at 8 cycles per
March 2025 amendment

Safety

Most common treatment-related adverse events (TRAEs)



63%
Neutropenia
20% grade 4



80%
Hypoalbuminemia



65%
Rash



81%
Paronychia

- **Grade 5 AEs occurred in 17% of patients** (11% treatment related: 5 infections, 1 pancreatitis).
- No further treatment-related deaths occurred after the **March 2025 amendment** capping pemetrexed at 8 cycles

Who benefits

Mutation type

Exon 19 deletion **70.8%**

L858R **60.0%**

HR 0.81 (80% CI, 0.46–1.42)

TP53 status

Altered **69.6%**

Not altered **66.9%**

HR 0.63 (80% CI, 0.34–1.18)

Brain metastases

None **72%**

Present at baseline **60.9%**

HR 2.00 (80% CI, 1.12–3.56)

Baseline ctDNA

Detected **68.0%**

Chemo alone **68.2%**

HR 0.82 (80% CI, 0.44–1.53)

Benefit held up broadly across biomarker subgroups. **Brain metastases** were the 1 factor tied to a statistically meaningful drop in PFS. In the harder-to-treat *TP53*-altered and ctDNA-detected groups, rates compared favorably with historical amivantamab + lazertinib alone (48.0% and 54.4% in the MARIPOSA subgroup analysis).

Why It Matters

AMIGO-1 is the first trial to test adding pemetrexed to the amivantamab/lazertinib doublet from MARIPOSA. The triplet cleared its 18-month PFS bar against historical osimertinib, and investigators flagged particular promise in poor-prognostic *TP53*-altered and ctDNA-detected patients. Toxicity — especially early treatment-related deaths before the pemetrexed cap — may have limited the regimen's full benefit; investigators say dose adjustments and prophylaxis could mitigate this in future evaluation.